

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A herpes simplex virus vector (HSV vector) that does not replicate in adult normal cells, that induces a viral gene expression and a viral replication specifically in a proliferating cells that express calponin, and that is capable of suppressing its replication at a desired timing by using the thymidine kinase gene, wherein the HSV vector is a recombinant HSV vector with a DNA fragment comprising:
 - (i) a promoter region ~~containing a full-length promoter~~ of the human calponin gene comprising the nucleotide sequence of SEQ ID NO.: 3;
 - (ii) the ICP4 gene encoding a transcription factor essential for initiation of a herpes viral replication which is integrated downstream of the promoter region ~~containing a promoter~~ of the human calponin gene,
 - (iii) the EGFP gene linked to the downstream of the ICP4 gene via an internal ribosomal entry site; and
 - (iv) the LacZ gene which is integrated upstream of said promoter region ~~containing the promoter~~ of the human calponin gene; ~~and~~
 - ~~(v) a thymidine kinase gene;~~

wherein the DNA fragment is inserted by recombination into the ribonucleotide reductase gene locus of the HSV vector that comprises an endogenous thymidine kinase gene and lacks functional endogenous ICP4 gene, and is not expressed or replicated in adult

normal cells, is capable of suppressing its replication at a desired period by using the thymidine kinase gene, and is obtained by the steps comprising: (i) inserting a DNA fragment comprising the ICP4 gene, the LacZ gene, the EGFP gene, and the region containing a promoter of the human calponin gene into the ribonucleotide reductase gene locus by a recombination; and (ii) using the expression of both the LacZ gene and the EGFP gene integrated in the vector are used as ~~an index~~ markers to identify the recombinant HSV vector.

- 2-5. (Cancelled)
6. (Currently amended) The HSV vector according to claim 1, wherein an enhancer is integrated upstream of the promoter region ~~containing a promoter~~ of the human calponin gene.
7. (Previously presented) The HSV vector according to claim 6, wherein the enhancer is a 4F2 enhancer.
- 8.-19. (Cancelled)
20. (Currently amended) A method for ~~expression/replication of~~ expressing a gene, protein or a peptide of a vector that is not ~~expressed/~~replicated in adult normal cells, comprising, introducing the HSV vector according to claim 1 into the cells and tissues of an organism, then expressing and replicating the gene, protein, or peptide of the vector.
21. (Currently amended) A method for suppressing the expression/~~replication~~ of a gene, protein or a peptide of the HSV vector according to claim 1 comprising,
- (i) introducing the HSV vector according to claim 1 into the cells and tissues of an organism,
 - (ii) expressing and replicating the gene, protein or peptide of the vector, and

- (iii) suppressing the expression ~~[[/]]~~ and replication of the vector at a later desired period by administering an antiviral drug, wherein said antiviral drug is aciclovir or ganciclovir.
22. (Cancelled)
23. (Cancelled)
24. (Cancelled)
25. (Currently amended) The method according to any one of claims 20 or 21 ~~[[to 24]]~~, wherein the cells and tissues in the organism are tumor tissues, vascular or lymphatic vessel constriction tissues, nephritic tissues or fibrotic tissues.
26. (Previously presented) A therapeutic drug comprising the HSV vector according to claim 1 wherein proliferating smooth muscle cells are targeted.
- 27.-34. (Cancelled)
35. (Currently amended) A method for producing a cell-specific HSV vector that does not replicate in adult normal cells, that induces a viral gene expression and a viral replication specifically in a proliferating cells that express calponin, and that is capable of suppressing its replication at a desired timing by using the thymidine kinase gene, said method comprising the steps of:
- (a) preparing a DNA fragment comprising,
- (i) a promoter region ~~containing a full length promoter~~ of the human calponin gene comprising the nucleotide sequence of SEQ ID NO.: 3,
- (ii) the ICP4 gene encoding a transcription factor essential for initiation of a herpes viral replication which is integrated downstream of the promoter region ~~containing said full length promoter~~ of the human calponin gene,

- (iii) the EGFP gene linked to the downstream of the ICP4 gene via an internal ribosomal entry site, and
- (iv) the LacZ gene integrated upstream the promoter region ~~containing the full length promoter~~ of the human calponin gene, ~~[[and]]~~
- ~~(v)—a thymidine kinase gene;~~
- (b) preparing recombinants by cotransfection with the HSV vector that comprises an endogenous thymidine kinase gene and lacks functional endogenous ICP4 gene together with the DNA fragment into a cell in which a promoter region of the human calponin gene that comprises the nucleotide sequence of SEQ ID NO.: 3 can be activated or a cell which expresses the human calponin gene inserting said DNA fragment into the ribonucleotide reductase gene locus by homologous recombination; wherein the DNA fragment is inserted by a homologous recombination into the ribonucleotide reductase gene locus of the HSV vector, and
- (c) ~~cotransfecting said DNA fragment within the ribonucleotide reductase gene locus with a viral DNA in a cell that activates the region containing the full length promoter of the human calponin gene or a cell that expresses the human calponin gene; and~~
- ~~——(d) purifying to screening a recombinant HSV vector and selecting a single clone of the HSV vector from the recombinants by limiting dilution without using agarose overlay assay using the expressions of both the LacZ gene and the EGFP gene as markers integrated in the HSV vector as an index, wherein said HSV vector is not expressed or replicated in adult normal cells and is capable of suppressing HSV Vector replication at a desired period by using the thymidine kinase gene.~~

36. (Previously presented) The method for producing the HSV vector according to claim 35, wherein the cell is an ICP4 (-) cell.